An explorative study for halting inflammation in patients with emphysema by administration of allogeneic bone marrow derived mesenchymal stromal cells.

Published: 06-02-2018
Last updated: 12-04-2024

Development of mesenchymal stromal cell therapy to halt the progression of emphysema.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON48907

Source
ToetsingOnline

Brief title
HEP study

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
COPD, stretched lungs

Research involving
Human

Sponsors and support

Primary sponsor: Longziekten

Source(s) of monetary or material Support: TAS ZonMW

Intervention

Keyword: bone marrow mesenchymal stromal cells (MSC), Emphysema, immune cell subsets, pulmonary microvascular endothelial cells (pMVEC)

Outcome measures

Primary outcome

Co-primary outcome parameters are: (1) to detect the difference in expression of PECAM-1 (CD31) on pulmonary microvascular endothelial cells (pMVECs) per micrometer alveolar septum present in lung tissue harvested from patients at LVRS 2 after 4 weeks of treatment with allogeneic MSC or placebo and (2) to measure the difference between MSC and placebo treatment in change in CO diffusion capacity over a period of 3 years following the second LVRS.

Secondary outcome

1. to demonstrate safety of i.v. administration of MSC to patients with moderate to severe emphysema as determined by WHO safety criteria.

2. the difference in expression of CD31 on pMVECs per micrometer alveolar septum present in lung tissue harvested from patients at lung surgery 2 (LVRS2) treated with placebo and patients treated with allogeneic MSC, recieved at 12 and 11 weeks prior to the surgery.

3. the difference in the number of CD3+ and CD4+ T-cells present in lung tissue harvested from LVRS 2 measured after administration of placebo or MSC at the two different time points as described in the protocol.

4. As in 2 and 3, but then the difference of these markers between LVRS 2 and 1 within patients.

5. the difference in the number of type II alveolar cells present in lung

tissue harvested from LVRS 2 from patients after 4 or 12 weeks of treatment

with placebo and patients treated with MSC.

6. The difference in shear stress response and level of apoptosis of isolated

pMVECs from LVRS 1 and 2 of patients treated with either MSC or placebo

7. The difference in Cytosplore response (explained below) of isolated immune

cells from LVRS 1 and 2 of patients treated with either MSC or placebo.

8. To demonstrate a statistical significant correlation between arterial pO2

or carbon monoxide gas exchange capacity at 12, 26 and 52 weeks after discharge

of admission for LVRS 2 and the outcome of the primary objective of the study

for patients treated with MSC.

Study description

Background summary

For patients with pulmonary emphysema there are no effective medications that can stop disease progression, even if they quit smoking. In recent years, success has been achieved with lungvolume reduction for pulmonary emphysema. By placing valves in airways, the patient becomes less short of breath. About 10% of all emphysema patients are eligible for treatment with valves. The alternative to another 10-20% of all emphysema patients is a surgical reduction of bullous parts in the lung, usually located in the top of the upper lung lobes of both lungs. If no more than 30% of all emphysema patients can be treated, this suggests that improvement of current emphysema treatment is highly needed.

Study objective

Development of mesenchymal stromal cell therapy to halt the progression of emphysema.

Study design

Double blind, placebo-controlled, randomized explorative study with allogeneic mesenchymal stromal cells cultured from bone marrow healthy donors.

Intervention

Patients undergo routine treatment for two lung-reducing operations (LVRS) with an interval of approximately 5 months. Patient will be randomized (2 : 1; MSC : placebo) for intravenous administration of a dose of 2 x 10> 6 MSC / kg body weight or placebo. These cells are administered prior to the second lung reduction operation, depending on the randomization result: 4 and 3 weeks before or 12 and 11 weeks prior to the second operation. Three months after discharge from the second LVRS, patients will be seen at the Outpatient Clinic of the Pulmonary Department of LUMC and at 6 monthly intervals for a total of 3 years. During each visit CO diffusion capacity will be measured. In addition, symptoms wil be recorded and phisical exam will be performed.

Study burden and risks

MSC is currently being investigated as cell therapy for a variaty of inflammatory diseases and agreement amongst clinical scientists is developing that MSC treatment is therapeutic because MSC have the ability to migrate to inflammatory sites to inhibit the local inflammatory response. It is remarkable that MSC appears safe for almost all diseases tested. As with all new medical treatments, it is important to accurately designed studies to find the right dose to identify an effect on relevant outcome measures. We have the strong opinion that MSC effects should first be analyzed in lung tissue of emphysema patients. Only after insight has been obtained in the anti-inflammatory effect by MSC in the lung tissue of emphysema patients, it will become clear to select the proper outcome parameters for future larger clinical trials. To date, it is not yet clear which outcome measures are most appropriate.
By using routine lungvolume-reducing surgery for treating emphysema, the burden of MSC treatment can be confined to a rather limited number of patients to investigate whether MSC cause anti-inflammatory effects in pulmonary emphysema.

Contacts

Public
Selecteer

Albinusdreef 2
Leiden 2300 ZA
NL
Scientific
Selecteer

Albinusdreef 2
Leiden 2300 ZA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1.Signed informed consent consistent with ICH-GCP guidelines and local legislation prior to participation in the trial.
2.Males or females between 45 and 65 years of age;
3.Emphysema as reported by a radiologist present in CT images of the lung; gradient of emphysema severity towards the lung apex as assessed by CT-derived lung densitometry by Pulmo CMS software (Medis, NL) and equally distributed between left and right lung.
4. Pre bronchodilator value measured FEV1 between 20% and 45% predicted; TLCO between 30% and 45% pred.; RV/TLC > 0.5.
5. Patients in a stable clinical condition.

Exclusion criteria

1. Significant cardiac failure;
2. active smoking, or < 6 months smoking cessation;
3. or failure to complete pulmonary rehab program before randomization;
4. women of child bearing potential;
5. any cancer treated in the previous 5 years;
6. women of child-bearing potential not using adequate contraception;
7. any other condition of the patient that the clinical investigator deemed harmful for study participation.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	21-06-2018
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Somatic cels allogenic

Ethics review

Approved WMO Date:	06-02-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-07-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Approved WMO Date:	27-08-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-001853-15-NL
CCMO	NL63261.000.17